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applicant's counsel. Applicant respectfully requests the PTO to examine each of these references and to so indicate on the enclosed PTO Form 1449.

Respectfully submitted,

Dated: September 12, 2002

Patrick F. Bright,
Reg. No. 24,318
BRIGHT & LORIG, P.C.
633 West 5th St., Ste 3330
Los Angeles, CA 90071
Tel: 213.627.7774
Fax: 213.627.8508
pbright@brightlorig.com

EXHIBIT A

2. A method of diagnosis and treatment of a disorder of the central nervous system of [the] a human [body that localizes] patient, other than a brain tumor, comprising:

localizing the disorder to the brainstem and limbic system of [the body.] said patient;

administering one or more drugs to said patient that block calcium intake channels of body cells;

administering one or more drugs to said patient that aid in inhibition of neural activity in the brain; and

monitoring said patient's response.

William E. Baumzweiger, M.D.
Neurology and Psychiatry
Tarzana Regional Medical Center
Cedars-Sinai Medical Center
Henry Mayo Newhall Memorial Hospital

Neuropathological Mechanisms Associated With Neurotoxic Exposure In Gulf War Veterans

Neuropathological Mechanisms Associated With Neurotoxic Exposure And Resulting Cranial Nerve Deficits, Abnormal Motor Activity and Pathological Reflexes Consistently Found In Neurotoxic States

Presentation to the Institute of Medicine
National Academy of Science
September 16, 1999
Washington, D.C.

18370 Burbank Blvd., Suite 204
Los Angeles, California, 91356

Oct. 16, 1999

Synopsis

Neurodysimmunity, commonly seen in what is commonly seen in what is called Gulf War Syndrome, is a neuro-immune/ Neuroinfectious / Neuropsychiatric disorder. It can be precipitated by infection, toxins, and inborn errors of Oxygen metabolism such as mitochondrial disease which initially involves the CNS, ANS, PNS, and then comes to involve Immune System. It then goes on to involve the other immune dominated organs, such as the gastrointestinal tract and lungs. It finally goes on to affect the ability to useitilize Oxygen on a tissue-level, with compramize of most tissue functions, butg particularly the lost of control over metabolic stress and the ability to fight off ifection. .

The source for the disorders seen in Gulf War Syndrome appears to be the brainstem and surrounding areas, , to which the critical symptoms localize. The third ventricle and brainstem area are crossroads of the information processing, encocirine, autonomic and corticospinal areas. They become involved in this dysregulation because of the infection and immune abnormalities caused by neurotoxic, traumatic and other insults to lymphocyte life cycle timing, allowing infective agents into the lymphocytes and glial cells, and transforming them from normal to abnormal activity.

Work to Date:
I have examined over 100 Gulf War veterans, and have treated over fifty, with very good success. I had noted in virtually all Gulf War veteran subjects exposed to various types of toxins that there are specific changes in the nervous systems of These patients have been exposed to a wide range of neurotoxic chemicals, fungi, viruses, to ionization of the atmosphere, radiation, and combinations thereof.

These changes are most prominently seen in the Cranial Nerves, axons of the CNS, and Peripheral Axons. The nature of neuronal injury due to neurotoxins--as discussed in the NATO report 1988- can lead to specific damage is specific areas, rather than a general encepalopathy. The type of neurotoxicity depends on the toxin, specific types of exposures leading to specific damage. The opposite scenario is more diffuse damage from more general attack on neural tissue leading to encephalopathy.

In terms of the specific type of neurotoxic injury, the brainstem with its cranial nerves are one very important area of specific injury. There is a tropism, based of genetic and membrane mechanism, as well as acetylcholine receptors for both virus (NATO Report of Neurotoxicity 1988). AND TOXIN

Energy Depletion and specificity of damage to circumscribed parts of the nervous system, OCCURS as well as immune damage. Specifically, there is damage to reverse transport. This mechanism typifies by organophosphate poisoning, which is one of our main concerns.

Oct. 16, 1999

1. Insecticide type organophosphate poisons become involved in injuries to the brain stem because of the large number of nicotinic acetylcholine receptors. Organophosphates act as hemi-substrates, which bind to the acetylcholinesterase enzyme, creating a stable, generally irreversible, inactive compound. This leads to accumulation of acetylcholine in the neuronal gap of the synapse. Acute intoxication by organo-phosphates first causes stimulation, then, later neurological depression, and finally coma.

At lower doses, accruing to more recent work, the specific deficits can appear without acute symptoms, except for headache, flu like symptoms and diarrhea. After exposure, there can be giddiness, subjective tension, restlessness, labile mood, insomnia, headache, tremor, nightmares, increased dreaming, apathy , withdrawal, confusion, slurred speech, generalized weakness.

Satoshi Ishikawa of Kitsato University has found the same convergence problems, difficulties with fixation, and decreased smooth pursuit found by this investigator.

The chronic effects seen in both studies in 1984 and in the Tokyo subway disaster of 1994 are polyneuropathies, drowsiness, lability of affect, apathy, fatiguability, anxiety and superinfection with pathogenic microbes.

In an early study in 1964, Gershown and Shaw showed visual-motor, memory and concentration deficits, which have been seen again in the Tokyo subway survivors.

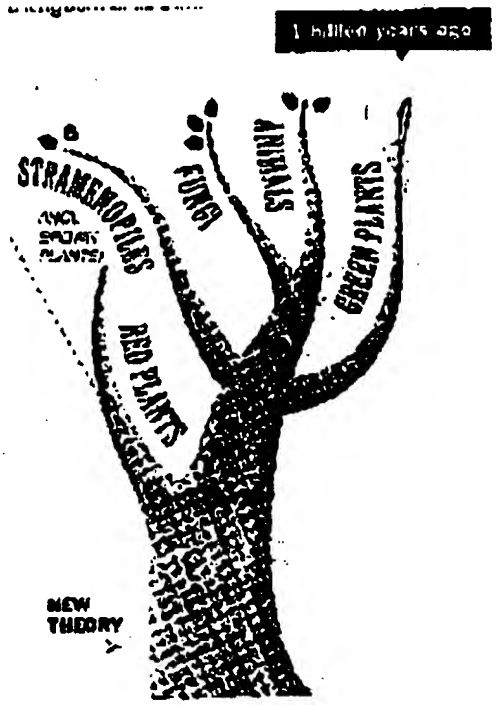
2. DNA Viruses ouch as Herpes are well known to infect neural tissue, but can remain latent in nerve tissue and reactivate (Neurovirology P.10), creating neurological and immunological problems. With EBV, the patient had bouts of fatigue low grade fever, hypersomnia, pain in hands and knees. EBV abnormal Sedimentation \ Rate and Rheumatoid Factor, spikes in the EEG.

One Patient had EBV virus titer with relapse. She developed beginning at this time difficulty with laying down new memories. She has had episodic dyscontrol (Personal Communication Richard Kaufman, M.D.) MHC Antigens were involved in an autoimmune reaction to create this damage. Combinations of EBV and head trauma created a progressive worse Neurotoxic syndrome in this Patient.

3. Fungi also appear to become involved in disease of the brainstem, as well as more generalized damage in severely

immunosuppressed individuals. Like the neural tissue, they emit electrical impulses (Shepherd) 1998. Many hundreds of fungi including Mucormycosis, Aspergillosis, coccidiomycosis, and Cryptococcus are relatively common CNS infections. They are found growing in the brainstem, in fact, found growing right out the front of the brainstem, into the sinuses and thence out the nose.

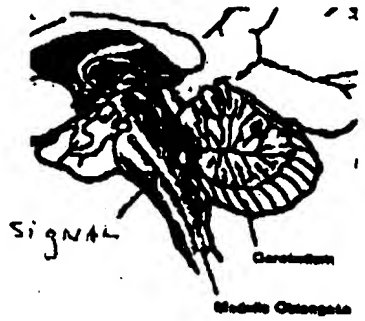
4. The most recent data on evolution demonstrate that fungi are the closest Genus to the animals, much closer than plants. This makes them even more likely to create autoimmune phenomena, and they obviously are able to produce some very toxic products, like the neurotoxic antibiotics:



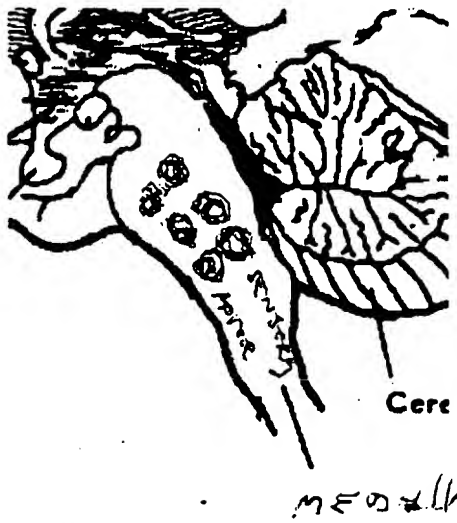
This creates two factors, first the human immune system has a much harder time keeping out fungi, especially if T Lymphocyte function is impaired, and secondly, the treatment of fungal infection is much more difficulty with anti-fungal treatment, which often causes many more allergic reactions and side effects, without complete eradication of the fungus. The relative closeness of fungi to animal life is one reason why they may be dangerously neurotoxic, through autoimmune mechanisms that would not arise from more distantly related life forms.

Thus, both viruses, which are neurotropic for the brainstem neurons, and fungi, which are from an evolutionary point of view the closest to animal, are the most difficult to eradicate. It is known that they are both left to the T Cell immune system to deal with (Parker's Textbook of Immunology).

Whatever the mechanism, the brainstem becomes inflamed, especially seen on the T- 2 sequence of the MRI, showing the motor and sensory nuclei highlighted with bright signnal.



Looking at this closer, on Magnified T 2 sequences of the MRI, one sees the following regarding the nuclei of the brainstem (3 motor nuclei and three sensory nuclei are pictured :



The nuclei of the brainstem are seen to be surrounded by yeast or inflammatory cells. They form a dark band. The white matter tracts of the brain and spinal cord, are specifically and typically involved. We will be discussing, due to the brief time, the brainstem, and the abnormalities seen in it. The red blood cell, and its mechanisms is clearly analogous to the axonal injury in neurons, and the injuries to supporting cells. However, we could have a very similar discussion about the peripheral and autonomic nervous systems, which are demonstrating consistant abnormalities.

In these patients, there was a consistent finding of diplopia close up and diplopia of color shift / dysmorphic change in the far field. I have recently come across the work of H. A. Solomon, OD, regarding the similarities and interplay of sympathetically controlled muscle verses-voluntary muscle control interactions. This interplay is greatly involved in convergence reflex's dynamic range.

There is a clear increase in cell death rates in Gulf War Syndrome and related syndromes. A defect in the failure to produce Growth Hormone which I saw in all patients may be part of the pathological process.

Insulin like Growth Factors are very important for the growth and maintenance of supporting cells, and even neurons. This is the basis for the stigmata of Neurodysimmunity. Ultimately, the liver, lung, heart smooth and striated muscles, thyroid, pancreas and peripheral nerves can become involved in this progressive autoimmune process.

The fact that so many disorders of control of brainstem systems occur in such a "temporal-geographical" sequence suggests that in this Syndrome diffuses through the brainstem, crossing through control systems which are proximal to the original pathology, to reach more distant systems.

This crossing over appears to be universal, but not always in the same sequence of involvement of brain operating systems. Further, the process can be started by various insults to the brainstem area, and is accelerated by combinations of these insults. The gaseous neuro-transmitters involved is, based on the data, the Nitric Oxide neurotransmitter system, which is more abundant in the brainstem then anywhere else in the body. The same is true for archived viral and fungal genes. Thus, neurodysimmunity is the result of multiple systems responding to toxic effects from multiple sources on first the nervous and immune systems, and then many of the operating organ systems of the entire body, one by one.

Neurodysimmunity is the result of multiple systems responding to toxic effects from multiple sources on first the nervous and immune systems. Then many of the operating organ systems of the entire body, one by one become involved in the disease process. Millions of our citizens are now at risk for this disease, truly on the brink, and need both diagnosis and treatment. There is an effective diagnostic protocol and a comprehensive treatment, which will be presented by this worker shortly.
In the nean time responsabible people must reserve jusgment, and turn to their best scientific advisiors instead of dismissing the complaints of Gulf War Veterans and whining.